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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/593,776	09/22/2006	Masato Fujioka	053466-0420	4182

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EXAMINER	
MERTZ, PREMA MARIA	
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1646	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/593,776	FUJIOKA ET AL.	
	Examiner	Art Unit	
	Prema M. Mertz	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15 and 31-45* is/are pending in the application.

4a) Of the above claim(s) *1-15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/22/06, 6/4/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election of Group II (claims 31-45, species: hearing loss caused by Meniere's disease) in the reply filed on 12/3/07 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 16-30 have been canceled (12/3/07). Elected claims 31-45 have been amended (12/3/07) and are under consideration by the Examiner.

Claims 1-15 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention.

Claim rejections-35 USC § 112, first paragraph, scope of enablement

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2a. Claims 31-45 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for treating Meniere's disease comprising administering an effective amount of IL-6 receptor antibody to a subject suffering from said disease, wherein the antibody administered is a monoclonal antibody PM-1 or MR16-1, does not reasonably provide enablement for a method for treating an inner ear disorder, comprising administering an IL-6 antagonist to a subject. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The specification delimits the instant method to administering antibodies PM-1 and MR16-1, however, claim 31 for example, recites a method for treating an inner ear disorder, comprising administering "an IL-6 antagonist" to a subject.

With respect to these claims, as recited, what is claimed in the instant invention broadly encompasses a method of administering "all" IL-6 antagonists. While the specification discloses that a "IL-6 antagonist" (see page 2, lines 30-31) is "for example" an anti-IL-6R antibody and this is the biological property which the administered compound is expected to exhibit, the specification is non-enabling for the unlimited number of compositions comprising "an IL-6 antagonist", and which are encompassed by the scope of the claims. Claim 31, for example, is a single means claim (M.P.E.P. 2164.08(a)). In In re Hyatt, 708 F.2d 712, 218 USPQ 195 (Fed. Cir. 1983), the Courts have held that: "A single means claim, i.e. where a means recitation does not appear in combination with another recited element of means, is subject to an undue breadth rejection under 35 U.S.C. 112, first paragraph." (A single means claim which covered every conceivable means for achieving the stated purpose was held nonenabling for the scope of the claim because the specification disclosed at most only those means known to the inventor). Since no material limitations for the IL-6 antagonist have been recited in the claim and only a biological activity has been recited, the claim encompasses every conceivable structure (means) for achieving the stated property (result), a fact situation comparable to Hyatt. Therefore, not only proteins, such as IL-6 antagonist peptides but antibodies against IL-6 and antibodies against the IL-6R, which exhibit an antagonist activity are encompassed by the scope of the claims. The claimed invention encompasses a method of administering compositions not envisioned or described in the specification, and neither does the specification disclose how these claimed

compositions can be distinguished from each other. The specification only enables treating Meniere's disease by administering PM-1 or MR16-1 antibodies, the antibodies having specific characteristics and properties. These properties may differ structurally, chemically and physically from other known proteins. By application of the factors set forth in Ex parte Forman (230 USPQ 546 (Bd. Pat. App. & Int. 1986), and reiterated in In re Wands (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)), which include (1) quantity of experimentation, (2) guidance presented, (3) the predictability of the art, and (4) the breadth of the claims, in the instant application, the quantity of experimentation to determine which other IL-6 antagonists to be administered are encompassed by the scope of the claims is practically infinite and the guidance provided in the specification very little, thereby rendering the results of the methods taught in the specification unpredictable (see pages 38-41). Therefore, it would require undue experimentation to determine which IL-6 antagonists to be administered in the claimed method would be encompassed by the scope of the claims. The disclosure of the two IL-6 receptor antibodies, is clearly insufficient support under the first paragraph of 35 U.S.C. § 112 for claims, which encompass every and all IL-6 antagonist. In In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970), the Courts have held that:

"Inventor should be allowed to dominate future patentable inventions of others where those inventions were based in some way on his teachings, since some improvements while unobvious from his teachings, are still within his contribution, since improvement was made possible by his work; however, he must not be permitted to achieve this dominance by claims which are insufficiently supported and hence, not in compliance with first paragraph of 35 U.S.C. 112; that paragraph requires that the scope of the claims must bear a reasonable correlation to scope of

enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific law; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved."

Furthermore, the amount of embodiments corresponding to the desirable compositions in the claimed method, may be innumerable, and the enabled embodiments amount to only two. Therefore, there are substantial scientific reasons to doubt the scope of enablement, as set forth above. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. The specification does not describe treatment of a disease other than treatment of inner ear disorders such as Meniere's disease by administering PM-1, and MR16-1 antibodies, and since it is deemed to constitute undue experimentation to determine all the others, the disclosure is not commensurate with the scope of the claims. It is suggested that by employing conventional claim language, the claims be amended to include the specific antibodies supported by the instant specification in the claimed method.

The following reference is cited herein to illustrate the state of the art with respect to antibodies:

Chuntharapai et al. (1997) note that the vast majority of antibodies are not antagonistic and that antibodies have to be screened to determine their ability to bind to human neutrophils (see page 21, second para). The reference also discloses that blocking activities of monoclonals

when compared show disparate blocking on ligand binding and inhibition of ligand binding or no inhibition at all (see page 24, last 2 lines; page 25).

Claim rejections-35 U.S.C. 112, second paragraph

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 31-45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 31 is vague and indefinite for several reasons.

Claim 31, line 2, is vague and indefinite because it recites "an IL-6 antagonist". The metes and bounds of the claim are unclear because it is unclear which of the numerous IL-6 antagonists claimed can be used in the treatment of the unknown disease.

Claim 31 is vague and indefinite because it is a method claim but fails to recite steps in the claim.

Claim 31 is vague and indefinite because it fails to recite that the subject is suffering from the disorder and an effective amount of the IL-6 receptor antibody is being administered to the patient suffering from the disorder.

Claim 31 is rejected as vague and indefinite because it fails to recite the specific disorder condition of the inner ear to be treated.

Claims 32-45 are rejected as vague and indefinite insofar as they depend on the above rejected claim for their limitations.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4a. Claims 31-39, are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 5,888,510 ('510 patent).

The '510 patent teaches a method of treating an IL-6 mediated disease such as rheumatoid arthritis by administering an IL-6 receptor antibody (see column 13-14, Example 2; column 14, claims 3-11).

With respect to the instant claims, the instantly claimed method would be an inherent property of the prior art method because in both methods an IL-6 antagonist is being administered. Newly discovered results of known processes directed to the same purpose are not patentable because such results are inherent. See MPEP. 2112-2112.02. See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d 1508 (CAFC 2001) in which the Court found that preamble language in claims of patents directed to administration of anticancer drug are expressions of purposes and intended results, and as such are non-limiting, since language does not result in manipulative difference in steps of claims. It does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure.

While the prior disclosure is silent as to the treatment of inner ear disorders by administration of an IL-6 antagonist, the instant claims merely recite a newly discovered result, i.e. treatment of inner ear disorders, a known method to the same use of IL-6 receptor antibody. The claimed process is not directed to a new use, it is the same use and it consists of the same method as described by the reference.

With respect to the claims, the IL-6 receptor antibody of the prior art would have the same effect as the instant claims when administered. Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established.

In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the prima facie case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. *In re Best*, 562 F.2d at 1255, 195 USPQ at 433. See also *Titanium Metals Corp. v. Banner*, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985) Once a reference teaching product appearing to be substantially identical is made the basis of a rejection, and the Examiner presents evidence or reasoning to show inherency, the burden shifts to the Applicant to show the difference.

Therefore, the method disclosed in reference meets the limitations recited in claims 31-39.

4b. Claims 31-43 are rejected under 35 U.S.C. 102(b) as being anticipated by EP 1074268 (2001).

The reference teaches a method of treating ulcerative colitis by administering IL-6 receptor antibodies, PM-1 and MR16-1, for the treatment of ulcerative colitis or Crohn's disease (see paragraph [0017], [0034]).

With respect to the instant claims, the instantly claimed method would be an inherent property of the prior art method because in both methods an IL-6 antagonist is being administered. Newly discovered results of known processes directed to the same purpose are not patentable because such results are inherent. See MPEP. 2112-2112.02. See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d 1508 (CAFC 2001) in which the Court found that preamble language in claims of patents directed to administration of anticancer drug are expressions of purposes and intended results, and as such are non-limiting, since language does not result in manipulative difference in steps of claims. It does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure.

While the prior disclosure is silent as to the treatment of inner ear disorders by administration of an IL-6 antagonist, the instant claims merely recite a newly discovered result, i.e. treatment of inner ear disorders, a known method to the same use of IL-6 receptor antibody. The claimed process is not directed to a new use, it is the same use and it consists of the same method as described by the reference.

With respect to the claims, the IL-6 receptor antibody of the prior art would have the same effect as the instant claims when administered. Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established.

In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the prima facie case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. *In re Best*, 562 F.2d at 1255, 195 USPQ at 433. See also *Titanium Metals Corp. v. Banner*, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985) Once a reference teaching product appearing to be substantially identical is made the basis of a rejection, and the Examiner presents evidence or reasoning to show inherency, the burden shifts to the Applicant to show the difference.

Therefore, the method disclosed in reference meets the limitations recited in claims 31-43.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5a. Claims 31-45 are rejected under 35 U.S.C. 103(a) as unpatentable over EP 1074268 (2001) in view in of Queen et al. (U.S. Patent No. 5,530,101).

The disclosure of EP 1074268 has been set forth above (see paragraph 4b above). However, the reference does not disclose administering humanized antibodies to IL-6R. Queen et al., (column 13, lines 5-65) teaches the humanization of monoclonal antibodies, as well as the issues involved in designing a humanized antibody that retains high affinity for its antigen. Queen et al., (column 17, lines 31-43) further teaches the production of antibody fragments, including the Fab fragment.

Therefore, at the time the invention was made, it would have been prima facie obvious to a person of ordinary skill in the art to obtain humanized antibodies as taught by Queen et al, to the IL-6R protein as taught by EP 1074268. The motivation for doing so would have been the

decreased immunogenicity of humanized antibodies when injected into humans, while the humanized antibodies retain their affinity for their epitope (Queen et al., (column 2, lines 5-8)).

Conclusion

No claim is allowed.

Claims 31-45 are rejected.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Prema Mertz whose telephone number is (571) 272-0876. The examiner can normally be reached on Monday-Friday from 7:00AM to 3:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on (571) 272-0835.

Official papers filed by fax should be directed to (571) 273-8300. Faxed draft or informal communications with the examiner should be directed to (571) 273-0876.

Information regarding the status of an application may be obtained from the Patent application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Prema Mertz/
Primary Examiner
Art Unit 1646